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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,501	09/26/2001	Daniel G. Chain	CHAIN-4A	1260

1444 7590 04/30/2004

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EXAMINER	
SPIVACK, PHYLLIS G	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 04/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,501	CHAIN ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicants' Response filed January 22, 2004 is acknowledged. In response to the request for an election of species, Applicants have elected the thiazolidinedione troglitazone.

Claims 1-30 are presented. Accordingly, the subject matter presently under consideration is a method for improving mental performance in patients having symptoms of reduced mental performance and are neither in a state of non-insulin dependent diabetes nor a state of general impaired glucose tolerance comprising administering an effective amount of the agent troglitazone to improve insulin sensitivity in the brain, claims 1-7, 10, 11, 15-25 and 27-30. Those methods of use comprising administering other agents are presently withdrawn from consideration by the Examiner, 37 CFR 1.142(b), as directed to non-elected inventions, claims 8, 9, 12-14 and 26. Re-affirmation of the election is requested when Applicants respond to this Office Action.

Three Information Disclosure Statements filed September 26, 2001, November 14, 2001 and March 10, 2004, respectively, are further acknowledged and have been reviewed.

Claims 1-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to improving mental performance in patients having symptoms of reduced mental performance and are neither in a state of non-insulin dependent diabetes nor a state of general impaired glucose tolerance comprising administering an effective amount of the agent

troglitazone to improve insulin sensitivity in the brain. The specification provides no more than hypothetical assertions that compounds that interact with the PPAR gamma, PPAR delta and PPAR alpha receptors, such as thiazolidinediones, agents known to improve both insulin sensitivity and brain glucose utilization, improve mental performance.

Attention is directed to In re Wands, 8 USPQ2d 1400 where the court set forth factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to improving mental performance in patients having symptoms of reduced mental performance and are neither in a state of non-insulin dependent diabetes nor a state of general impaired glucose tolerance comprising administering an effective amount of the agent troglitazone to improve insulin sensitivity in the brain.

The relative skill of those in the art is generally that of a Ph.D. or M.D. with expertise in the fields of endocrinology and/or neurology.

Each particular endocrine or neurologic disease or disorder involving cognition or memory has its own specific characteristics and etiology. The broad recitation "improving mental performance" is inclusive of many conditions that presently have no established successful therapies.

It is clear the art to which the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy.

The breadth of the claims

The claims are very broad in that they are inclusive of any disease and disorder characterized by diminished mental performance wherein a patient has symptoms of reduced mental performance but is neither in a state of non-insulin dependent diabetes nor a state of general impaired glucose tolerance comprising administering troglitazone.

The amount of direction or guidance provided and the presence or absence of working examples

There are no working examples directed to the administration of troglitazone to improve mental performance.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to which particular thiazolidinedione would be preferred for improvement of the many diseases or disorders of the brain that are characterized by diminished mental performance. The skilled artisan would expect the administration of a particular agent to improve mental performance to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for the agent. The instant specification sets forth no such understanding nor any criteria for extrapolating beyond what is known in the prior art. There is no support provided wherein a patient population having symptoms of reduced mental performance, and neither in a state of non-insulin dependent diabetes nor a state of general impaired glucose tolerance, demonstrated improvement of mental performance following administration of an effective amount of the agent troglitazone to improve insulin sensitivity in the brain. Absent reasonable *a priori* expectations of success for using a particular chemotherapeutic agent to improve mental performance, one skilled in the neurology art would have to test extensively many agents to discover which shows efficacy in improving mental performance. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 10, 11, 15-25 and 27-30 rejected under 35 U.S.C. 103(a) as being unpatentable over Wickelgren, I., Science.

Wickelgren's disclosure is directed to the beneficial role that insulin serves to improve memory and enhance cognition. See the bottom of the third column on page 518 where troglitazone (Rezulin) is specifically suggested as an agent to counteract memory loss by correcting insulin resistance. Wickelgren fails to recite patients who are in a state of non-insulin dependent diabetes nor a state of general impaired glucose tolerance, as required by the present claims. The claims differ in that Wickelgren fails to disclose the areas of the brain associated with mental performance or memory, the relationship of troglitazone to a PPAR receptor or the insulin transduction process, the administration of an additional agent to improve mental performance or the additional administration of egressin. However, egressin is known in the prior art as an aid in the transport of drugs across the blood brain barrier to increase glucose metabolism. Acetyl-L-carnitine is established in the prior art as an agent to improve learning ability, memory and attention in the elderly. Further, troglitazone, as a thiazolidinedione, is known in the prior art to be an agent that improves insulin sensitivity, improves glucose utilization and interacts with the peroxisome proliferator-activated receptor in glial cells.

Thus the claims are denied.

Any inquiry concerning this communication should be directed to Phyllis G. Spivack at telephone number 571-272-0585.

Phyllis Spivack

Phyllis G. Spivack
Primary Examiner
Art Unit 1614

April 28, 2004

PHYLLIS SPIVACK
PRIMARY EXAMINER